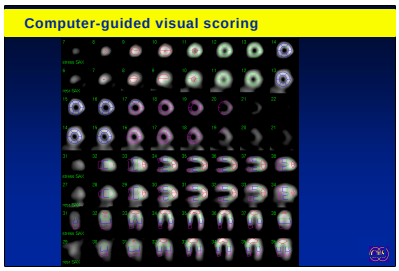
COURAGE Chronicle

August 2000

Nuclear Substudy II Getting Underway



Nuclear Substudy II (NSII) is designed to look at the short-term effects of medical and interventional therapy on ischemic burden as determined by myocardial perfusion SPECT imaging.

Inclusion Criteria: Patients must have moderate to severe ischemia measured as a summed difference score [SDS] of ≥ 5 on the baseline stress nuclear scan to be eligible for enrollment in *NSII*. Prior to entry into NSII, the extent of ischemia and the technical adequacy of the baseline study are subject to verification by the Cedars-Sinai core laboratory.

Medications During SPECT: ***At pre-randomization it is preferred that patients be off all anti-ischemic medications during their SPECT scan so that the extent and severity of the ischemia shown will be maximized, increasing the chances that the patient will have the required amount of ischemia to meet the eligibility requirements for NSII.*** **Prior to the baseline SPECT**, a patient should be off calcium channel blockers for at least 24 hours and off long-acting nitrates for at least six hours. If clinically feasible, all beta-blockers should be discontinued at least 48 hours prior to the baseline SPECT. **Prior to the follow-up SPECT**, a patient should **not** be taken off their medications. Since the goal of this substudy is to determine whether intensive medical therapy reduces the amount of ischemia, patients should continue their usual medication regime prior to the follow-up SPECT.

Timing of Follow-Up SPECT: The follow-up SPECT should be 60-120 days following the date of the initial treatment (PCI or start of new intensive medical therapy). This time period is long enough to minimize residual ischemic defects that can be seen early post-angioplasty and to allow improvement in endothelial function (and probably myocardial perfusion) after initiation of intensive medical therapy. In addition, this time period should be short enough to minimize patient dropout from *NSII* due to clinical events prior to the follow-up SPECT scan.

Patients with Worsening Symptoms Prior to the 60 to 120-day Follow-Up Period: If a patient has severe symptoms that warrant subsequent intervention, we encourage the investigator to attempt to stabilize the patient and perform a SPECT scan prior to intervention, if clinically safe. Our goal is to include such a patient in *NSII* even though the SPECT scan is performed prior to the 60 to 120-day follow-up window.

Tc-99m Sestamibi and Adenosine: Tc-99m sestamibi (Cardiolite) and adenosine (Adenoscan) will be provided for the substudy at no charge.

IRB/Ethics Approval: Because *NSII* involves a procedure (follow-up SPECT) that is not dinically indicated and not described in the main trial protocol, this substudy requires its own IRB/Ethics Committee approval, independent of the IRB/Ethics Committee approval for the main COURAGE Trial. In addition, your institution may require a radiation safety approval since this protocol includes radioactive imaging agents. For more information, please call Kate Hanson (ph: 404-727-9235, or email: kjhanso@sph.emory.edu) at Emory or Tara Gurtler (ph: 310-423-4387) at Cedars-Sinai. We can provide you with a protocol, a template informed consent and other information.

Stress Test Requirement at One Year

A stress test is required at the 12 and 36 month visit. A modified symptom-limited exercise with gated sestamibi SPECT imaging is preferred or a pharmacological stress in patients unable to exercise. **However, an exercise stress test is acceptable.** Please complete Form 6 and/or 7 as appropriate.

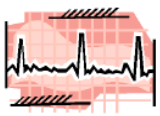
Albuquerque Update.

- Packaging Update: Adenoscan® (Adenosine) 3mg/mL will no longer be provided in individual unit-of-use bags. The vials will continue to be shipped in the commercial boxes with the appropriate warning label information, but the investigational label will now be placed on the outside of the shipping box instead of on the individual bags.
- Please use the new COURAGE DRUG ORDER FORM to order additional supplies of study meds. ***Please note that medications will not be shipped unless an order form is received.***
- All BULK DRUG DISPENSING RECORDS included in each box of study medication must be completed and returned to the Pharmacy Coordinating Center. These forms provide the pharmaceutical companies with the necessary documentation for accountability of drug dispensation.

IRB Approvals

Please send the IRB approvals of Protocol Amendments Nos. 1 & 2, and the Annual Extension for your site's continuation in the COURAGE Trial to Joan Smith at the West Haven Coordinating Center .

ECGs



Please send *original* ECGs to West Haven, and remember that all ECGs must be 'blinded' with the only identification being the patient's seven digit ID Number to protect patient confidentiality.

PATIENT ENROLLMENT UPDATE

		To Date	Since Annual Meeting
671	Audie L. Murphy VAMC – San Antonio	65	30
202	London Health Sciences Centres	42	27
580	Houston VA Medical Center	36	16
203	Montreal Heart Institute	35	24
È	***WEEK 60: TARGET ENROLLMENT per SITE:***	***35***	***17***
506	Ann Arbor VA Medical Center	32	9
558	Durham VA Medical Center	27	8
205	Queen Elizabeth II HSC	26	19
209	Sunnybrook & Women's College HSC	24	18
598	John C. McClellan VA – Little Rock	24	14
306	Mayo Clinic—Rochester	22	15
630	New York VA Medical Center	21	17
200	Foothills Hospital	20	14
596	Lexington VA Medical Center	20	12
663	Seattle VA Medical Center	17	9
308	Mid America Heart Institute/Shawnee Mission	17	5
584	Iowa City VAMC/Univ. of Iowa Hospital	15	11
312	University of Michigan Medical Center	16	12
313	University of Oklahoma	14	8
304	Emory University Hospital	14	7
501	Albuquerque VA Medical Center	14	7
210	The Toronto Hospital	14	7
212	Vancouver Hospital & Health Science Centre	12	12
626	Nashville VA Medical Center	12	8
301	Boston Medical Center	9	7
211	University of Alberta Hospital	9	6
204	St. Michael's Hospital	8	8
207	St. Paul's Hospital	8	6
201	Hamilton General Hospital, McMaster Clinic	8	5
314	MIMA Century Research Associates	6	6
208	Sudbury Memorial Hospital	5	4
300	Barnes-Jewish Hospital	3	3
626	Vanderbilt University Medical Center	3	3
648	Portland VA Medical Center	3	3
***	All Terminated Sites	18	5

Total Patients as of 08/18/2000: 622

Avoiding Recidivism

For the first three months of the trial, COURAGE patients have made great strides in improving their diet and exercise regimes. However, during the three month hiatus after their third follow-up visit some patients have slipped back to earlier, less healthy routines. All Coordinators need to strongly encourage their patients to take control of managing their own health by taking their meds and *keeping to their diet, exercise and smoking cessation plans for the upcoming three - and six-month breaks between visits.*